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IN REPLYING, ADDRESS THE

Tbc. Research Laboratory,
411 E. 69th St., New York 21, N. Y.

May 10, 1949.

Dr. Joshua Lederberg,
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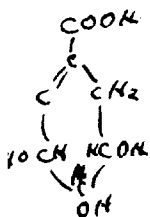
Dear Josh:

We have finally got around to testing our triple and quadruple aromaticless mutants. Over a dozen phenolic compounds, as well as cyclohexane carboxylic acid and cyclohexanol plus serine, have been tested. None of these could be substituted for the triple or the quadruple requirements. Shikimic acid, however, which was recently furnished by Stanier, permitted as rapid growth of the quadruple mutant as did an excess of the three aromatic amino acids and PABA. It is not used by the triple mutant. On either of these media the ~~triple~~ quadruple mutant is quite slow. The quadruple mutant grows practically as rapidly as wild type on a mixture of the three aromatic amino acids plus ~~PABA~~. This suggests the possibility that shikimic acid may be a precursor of PABA plus an unknown compound, and is less readily available by reversal of the normal process to form the precursor of the three aromatic amino acids. Incidentally, quinic acid, which is simply shikimic acid with a dehydrated double bond, does not work.

Tyr + Phe + Trp

This seems to me to be very strong evidence in favor of the notion, suggested in your letter of January 29th, that the benzene ring is synthesized ~~by~~ a cyclohexyl derivative. It is of particular interest since H. O. L. Fischer found that shikimic acid can be oxidized by chemical means to trans-aconitic acid, and Stanier (J. Bact. 55, p. 489, April 1948) has suggested the possibility of synthesis of the benzene ring by reversal of this process. I have wondered what you are planning to do with the observations you and Zinder have made on your aromaticless Salmonella mutant. I would like to have a biochemist here next year go into our several aromaticless mutants in detail, especially since the mutant which requires only the three aromatic amino acids feeds the one which requires PABA. As it is not yet certain that we will be able to go into this problem as extensively as I had hoped, I am inclined toward publishing a brief paper on this shikimic acid observation, as it may be of some interest to biochemists working with aromatic compounds. Since you have been working along parallel lines, I wonder if you would care to publish your results at the same time, or whether you would like to

shikimic.



Shikimic acid

Dr. Joshua Lederberg

May 10, 1949.

have me refer to any of your material, either in press or unpublished. I would rather write my stuff up as ^{something} slightly longer than a letter to the Editor.

Since your aromaticless Salmonella mutant responds to a variety of phenols and to cyclohexanol plus serine, I presume it is blocked at a different place from our aromaticless E. coli mutant, altho it also seems possible that the Salmonella may carry out certain conversions more reversibly. For example, you have isolated a Salmonella mutant that responds to phenylalanine or tyrosine, while we have an E. coli mutant (and Howard Mueller has found a number of mutants in K-12) which require both phenylalanine and tyrosine. I would appreciate knowing which are the phenols that your aromaticless Salmonella responds to and whether you believe these are intermediates in the normal path of synthesis of the known aromatic metabolites. Furthermore, since our triple mutant feeds our quadruple mutant, it would be interesting to know whether any syntrophic relationship exists between your mutant and any of ours. Would you be able to send me your strain for this purpose -- is it by any chance the SW-38 labelled "phenylalanine or tyrosine, very unstable" which you have already sent me?

*for growth,
slow growth
on either
alone.*

I am extremely sorry not have have got around to any recombination studies which I had formerly intended, but I do hope we will do a little during the next month before leaving for the summer in Pacific Grove.

If you want a little shikimic acid, I would be glad to send some, as well as our aromaticless mutants, if you want to make any comparisons.

With best regards to Esther,

Sincerely,

B.D.D.

Bernard D. Davis

BDD/hl

P.S. - Paper chromatography has recently confirmed microbiological evidence that a tyrosine mutant spills out phenylalanine and that a phenylalanine ^{mutant} spills out tyrosine, and a mutant blocked early in isoleucine synthesis (which responds to alpha-amino-butyric acid) spills out valine. In addition, ninhydrin shows ^{large} spots as well! It looks as though the interactions between parallel synthetic paths will be very complicated indeed.

I enjoyed your review very much.

B.D.D.